



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/647,156

08/22/2003

Dirk Stenkamp

01-1387

1272

28501

7590

09/11/2008

MICHAEL P. MORRIS

BOEHRINGER INGELHEIM USA CORPORATION

900 RIDGEBURY ROAD

P. O. BOX 368

RIDGEFIELD, CT 06877-0368

EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

09/11/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/647,156	<b>Applicant(s)</b> STENKAMP ET AL.	
	<b>Examiner</b> TAMTHOM N. TRUONG	<b>Art Unit</b> 1624	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 June 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 45-59, 61, 63, 64, 66 and 67 is/are pending in the application.
- 4a) Of the above claim(s) 69-73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 45-59, 61, 63, 64, 66, and 67 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### NON-FINAL ACTION

Applicant's amendment of 6-2-08 has been considered. The amended claims have overcome the previous rejections of 112/1st and 2nd paragraphs. However, in view of the species disclosed in the specification, the following enablement rejection is necessary.

Claims 1-44, 62, 65 and 68 are cancelled.

Claims 69-73 are held withdrawn as per previous office action.

Claims 45-61, 63, 64, 66 and 67 are pending.

#### *Claim Rejections - 35 USC § 112, Second Paragraph*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 45-61, 63, 64, 66 and 67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 45 recites "Carboxamide **compounds comprised of...**" The plural term "compounds" is not proper because it suggests a mixture of compounds rather than a single compound as intended. Further the "comprised of" language in a compound claim is open-ended and permits limitations outside the scope of the intended formula.

Applicant is suggested to adopt the language of "A carboxamide compound of formula I.1".

- b. Claim 45 recites “U, V **independent of one another** denote CH”. The phrase “independently of one another” is unnecessary because both terms represent the same thing (i.e., CH).
- c. Claim 45 recites “...compounds...and the salts thereof”;  
Claim 60 recites “...compounds...and the **pharmaceutically** acceptable salts thereof”;  
Claim 61 recites “The **physiologically** acceptable salts”;  
Claim 66 recites “...a pharmaceutically acceptable salt thereof”;  
There is inconsistency between independent claim and dependent claims regarding the type of salts.
- d. Claim 53 lacks antecedent basis because it depends on claim 45, but recites U as a nitrogen, which is not in claim 45.
- e. Claims 53-55 recite that “...V denotes a C atom”, “...U denotes a C atom”, “...U and V each denote a C atom”. Said recitations are inconsistent with claim 45 which recites “U,V independently of one another denote **CH**”. Applicant is suggested to adopt the language of claim 45.  
  
Claim 55 would be a substantial duplicate of claim 45 if “CH” replaces “a C atom”.
- f. Claim 54 lacks antecedent basis because it depends on claim 45, but recites V as a nitrogen, which is not in claim 45.

g. **Use claim:** Claim 67 provides for the use of a carboxamide compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

#### ***Claim Rejections - 35 USC § 101***

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

**Use Claim:** Claim 67 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

#### ***Claim Rejections - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Scope of Enablement:** Claims 45-59, 61, 63, 64, 66 and 67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using compounds of formula I.1 wherein  $-NR^1R^2$  is *pyrrolidinyl, piperidinyl, morpholino* or *dialkylamino*, does not reasonably provide enablement for making and using compounds of formula I.1 wherein  $-NR^1R^2$  is another moiety (e.g., piperazinyl, azipinyl, etc.). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

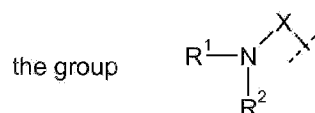
- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

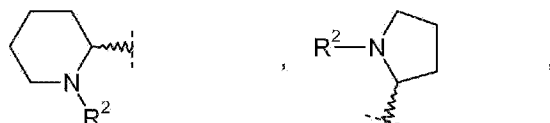
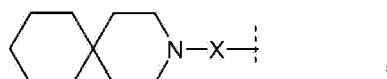
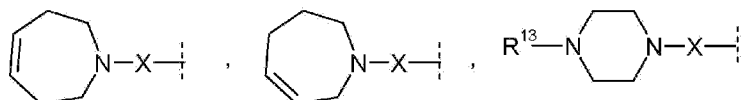
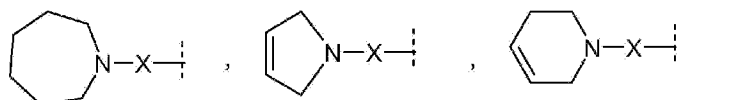
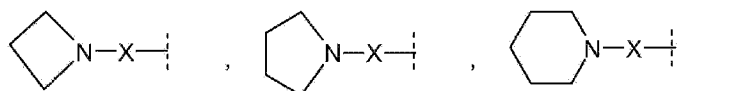
**The breadth of the claims:** The scope of  $-NR^1R^2$  covers an extensive list of moieties ranging from simple ones such as: amino, alkylamino to a variety of rings, see the following excerpt:

Art Unit: 1624

$R^1, R^2$  independently of one another denote H, a  $C_{1-8}$ -alkyl or  $C_{3-7}$ -cycloalkyl group optionally substituted by the group  $R^{11}$  or a phenyl group optionally mono- or polysubstituted by the group  $R^{12}$  and/or monosubstituted by nitro, or



is defined according to one of the following partial formulae



wherein one or more H atoms of the heterocycle formed by the group  $R^1R^2N$ - may be replaced by  $R^{14}$  and the ring connected to the heterocycle formed by the group  $R^1R^2N$ - may be mono- or polysubstituted at one or more C atoms by  $R^{20}$ , and in the case of a phenyl ring may also

Note, the above heterocycles can also be substituted with other groups such as  $R^{14}$  and  $R^{20}$ . Thus, the scope of formula I.1 is unduly broad and goes beyond the intended biphenyl-(phenyl-ethyl)amide.

**The amount of direction or guidance presented:** The specification provides a generic process for making compounds of formula I.1 wherein  $-NR^1R^2$  is a *pyrrolidinyl* ring. The process does not teach how other rings can be added to the quinazoline ring, nor does it teach how  $R^1$  and  $R^2$  can form a ring. Particularly, the specification is silent with regard to starting materials for making compounds with such a broad range of heterocycles represented by  $-NR^1R^2$ . With working examples are limited to a few specific rings for  $-NR^1R^2$  (e.g., *pyrrolidinyl*, *piperidinyl*, *morpholino*), the skilled chemist would not be able to extrapolate from the synthetic procedures of the disclosure to make compounds of formula I.1 with other moieties instantly claimed for  $-NR^1R^2$ . Furthermore, the established biological activity for the species made cannot be extrapolated to other compounds of formula I.1 due to the different structural attributes of the diverse moieties claimed for  $-NR^1R^2$ . Thus, the specification fails to provide adequate guidance for making and using the claimed compounds with such complex ring systems and divergent structure.

**The state of the prior art:** There is no reference presented on record or found in the prior art where a biphenyl-(phenyl-ethyl)amide is substituted with another group such as: azepine, spirocycle, or with such an extensive and diverse selection of substituents such as those claimed herein. Thus, there is no guidance in the art or provided in the instant disclosure to substantiate such diversity for making and using compounds such as those instantly claimed.



**The relative skill of those in the art:** Even with advanced training, the skilled artisan would have to carry out extensive research to select an effective compound from the large Markush group of compounds represented by formula I.1. Not only does one have to determine an  $IC_{50}$  value, but also *in-vivo* activity or some other art accepted correlative procedures to establish an  $LD_{50}$ , therapeutic indexes and pharmacokinetic profiles for the compounds of the genus. Given such a large Markush group of compounds for formula I.1, such a task would require a tremendous amount of effort, time and resources. The examiner establishes herein these tasks would indeed impose an undue burden upon a person attempting to practice this invention.

**The predictability or unpredictability of the art & The quantity of experimentation necessary:** Unpredictability in the pharmaceutical arts has been well established due to various and often conflicting biochemical pathways and complex biological factors that often affect conditions in an individual on a case by case basis. In the instant case, the specification has not provided sufficient support or guidance to shown how to make the compounds of general formula I.1 with the extensive substitution profile asserted with complicated rings or ring systems and functional groups representative of the scope asserted for the  $-NR^1R^2$  moieties, much less establishing biological activity for such a broad range of generic compounds, especially as the structure diverges so much that activity recognized for the core may be and is questioned.

Thus, given the unpredictable nature of the art, the deficiencies of the disclosure and the vast array and diverse compounds claimed herein, one skilled in the art would indeed be forced

Art Unit: 1624

to engage in undue experimentation to make and use compounds of formula I.1 as recited in the claims as currently drafted.

### ***Claim Objections***

4. Claim 60 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 60 recites species of biphenyl-(phenyl-ethyl)amide substituted with a group represented by  $-NR^1R^2$  that is not taught or fairly suggested by the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Tamthom N. Truong/

/Deepak Rao/  
Primary Examiner  
Art Unit 1624

***Tamthom N. Truong***  
***Examiner***  
***Art Unit 1624***

9-9-08